REMARKS

I. Claims in the Case

Claims 9, 10, 15 and 16 have been amended. Claims 62-74 have been added. Claims 1-8, 11-14, 18-35, 44-45 and 50-61 are withdrawn. Claims 9-10, 15-16, 36-43, 46-49 and 61-74 are under examination.

II. Amendments

Claims 9, 10, 15 and 16 have been amended in a manner to address the Section 112 and 102 concerns.

For example, the claims now recite a polypeptide being at least 50 or 75 amino acids shorter than SEQ ID NO:2. This amendment is intended simply to distinguish the claimed fragments from the full-length apo-A-I sequence that is known in the art. Support for the fact that the present invention was intended to embrace "fragments" of apo-A-I, wherein the apo-A-I fragments have a 50 or 75 or more amino acid size reduction as compared to apo-A-I (*i.e.*, SEQ ID NO:2) can be found in the specification at paragraph [0073].

To address written description and enablement concerns, certain of the claims also now recite embrace polypeptides having high degree of sequence identity, at least 85%, 90% or 95% amino acid identity, to SEQ ID NO:2. Support for this language can be found at paragraphs [0083] and [0109].

The new claims are merely narrowing dependent claims.

III. Enablement and Written Description Rejections

It is believed that the foregoing amendments fully resolve the enablement and written description concerns by removing the "consisting essentially of" language.

For example, claims 9 and 16 are now directed to a vector comprising a nucleic acid molecule "consisting of" the specified nucleotide sequences. This was done to resolve the uncertainty and concerns with respect to the previous "consisting essentially of" transition phrase. It is noted that the vector is still open to the inclusion of any of a number of additional elements, even additional coding sequences, so long as the vector includes at least the specified nucleotide sequence. This amendment is in accordance with recent Board of Appeals and Federal Circuit caselaw, as discussed below.

Claim 15 has replaced the "consisting essentially of" language with "comprising", which is in accordance with recent caselaw discussed below.

Applicants would further point out that new claims 63, 67 and 71 exclude the "% identity" language altogether and thus should clearly be acceptable with respect to written description and enablement.

The claims are now in accordance with recent written description and enablement cases out of the Court of Appeals for the Federal Circuit, including for example the Federal Circuit's recent decision in *Capon v. Eshhar v. Dudas*, 418 F.3d 1349, 76 USPQ2d 1078 (Fed. Cir. 2005). As the *Capon* court points out, there is no requirement under section 112 that a specification contain a detailed description of elements where those elements are well known to those in the field:

> The Board stated that "controlling precedent" required inclusion in the specification of the complete nucleotide sequence of "at least one" chimeric gene. Bd. op. at 4. The Board also objected that the claims were broader than the specific examples. Eshhar and Capon each responds by pointing to the scientific completeness and depth of their descriptive texts, as well as to their illustrative examples. The Board did not relate any of the claims, broad or narrow, to the examples, but invalidated all of the claims without analysis of their scope and the relation of claim scope to the details of the specifications.

Eshhar and Capon both argue that they have set forth an invention whose scope is fully and fairly described, for the nucleotide sequences of the DNA in chimeric combination is readily understood to contain the nucleotide sequences of the DNA components. Eshhar points to the general and specific description in his specification of known immune-related DNA segments, including the examples of their linking. Capon points similarly to his description of selecting DNA segments that are known to express immune-related proteins, and stresses the existing knowledge of these segments and their nucleotide sequences, as well as the known procedures for selecting and combining DNA segments, as cited in the specification.

Both parties argue that the Board misconstrued precedent, and that precedent does not establish a *per se* rule requiring nucleotide-by-nucleotide re-analysis when the structure of the component DNA segments is already known, or readily determined by known procedures. The "written description" requirement implements the principle that a patent must describe the technology that is sought to be patented; the requirement serves both to satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed. See *Enzo Biochem*, 296 F.3d at 1330 (the written description requirement "is the *quid pro quo* of the patent system; the public must receive meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time"); *Reiffin v. Microsoft Corp.*, 214 F.3d 1342, 1345-46 (Fed. Cir. 2000) (the purpose of the written description requirement "is to ensure that the scope of the right to exclude . . . does not overreach the scope of the inventor's contribution to the field of art as described in the patent specification"); *In re Barker*, 559 F.2d 588, 592 n.4 (CCPA 1977) (the goal of the written description requirement is "to clearly convey the information that an applicant has invented the subject matter which is claimed"). The written description requirement thus satisfies the policy premises of the law, whereby the inventor's technical/scientific advance is added to the body of knowledge, as consideration for the grant of patent exclusivity.

The descriptive text needed to meet these requirements varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence. The law must be applied to each invention that enters the patent process, for

each patented advance is novel in relation to the state of the science. Since the law is applied to each invention in view of the state of relevant knowledge, its application will vary with differences in the state of knowledge in the field and differences in the predictability of the science.

For the chimeric genes of the Capon and Eshhar inventions, the law must take cognizance of the scientific facts. The Board erred in refusing to consider the state of the scientific knowledge, as explained by both parties, and in declining to consider the separate scope of each of the claims. None of the cases to which the Board attributes the requirement of total DNA re-analysis, *i.e.*, *Regents v. Lilly*, *Fiers v. Revel*, *Amgen*, or *Enzo Biochem*, require a re-description of what was already known. In *Lilly*, 119 F.3d at 1567, the cDNA for human insulin had never

been characterized. Similarly in *Fiers*, 984 F.2d at 1171, much of the DNA sought to be claimed was of unknown structure, whereby this court viewed the breadth of the claims as embracing a "wish" or research "plan." In *Amgen*, 927 F.2d at 1206, the court explained that a novel gene was not adequately characterized by its biological function alone because such a description would represent a mere "wish to know the identity" of the novel material. In *Enzo Biochem*, 296 F.3d at 1326, this court reaffirmed that deposit of a physical sample may replace words when description is beyond present scientific capability. In *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1332 (Fed. Cir. 2003) the court explained further that the written description requirement may be satisfied "if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." These evolving principles were applied in *Noelle v. Lederman*, 355 F.3d 1343, 1349 (Fed. Cir. 2004), where the court affirmed that the human antibody there at issue was not adequately described by the structure and function of the mouse antigen; and in *University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 925-26 (Fed. Cir. 2004), where the court affirmed that the description of the COX-2 enzyme did not serve to describe unknown compounds capable of selectively inhibiting the enzyme.

The "written description" requirement must be applied in the context of the particular invention and the state of the knowledge. The Board's rule that the nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known, is an inappropriate generalization. When the prior art includes the nucleotide information, precedent does not set a *per se* rule that the information must be determined afresh. Both parties state that a person experienced in the field of this invention would know that these known DNA segments would retain their DNA sequences when linked by known methods. Both parties explain that their invention is not in discovering which DNA segments are related to the immune response, for that is in the prior art, but in the novel combination of the DNA segments to achieve a novel result.

The "written description" requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution. Both Eshhar and Capon explain that this invention does not concern the discovery of gene function or structure, as in Lilly. The chimeric genes here at issue are prepared from known DNA sequences of known function. The Board's requirement that these sequences must be analyzed and reported in the specification does not add descriptive substance. The Board erred in holding that the specifications do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes.

Applicants highlight a quote from the preceding passage: "None of the cases to which the Board attributes the requirement of total DNA re-analysis, *i.e.*, *Regents v. Lilly*, *Fiers v. Revel*, *Amgen*, or *Enzo Biochem*, require a re-description of what was already known." While *Capon* dealt with DNA sequences *per se*, we submit that the reasoning is fully consistent with the present case, which also concerns the amino acid sequences.

The Capon case has very recently been followed by the Federal Circuit, in *Falkner v. Inglis*, App. No. 05-1324, decided May 26, 2006 (Fed. Cir. 2006) (copy enclosed). The *Falkner* court, following the *Capon* decision, stated:

> Indeed, a requirement that patentees recite known DNA structures, if one existed, would serve no goal of the written description requirement. It would neither enforce the quid pro quo between the patentee and the public by forcing the disclosure of new information, nor would it be necessary to demonstrate to a person of ordinary skill in the art that the patentee was in possession of the claimed invention. ... Accordingly, we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here "essential genes"), satisfaction of the written description requirement does not require either the recitation or incorporation by reference (where permitted) of such genes and sequences.

Id. at page 17-18. The court's reasoning in *Falkner* is directly applicable to the present case.

The amino acid "substitution, deletion" *etc.* language has been removed from the claims, and the claims have been newly formulated with amino acid "identity" language specifically found acceptable in the PTO Guidelines and recent Board of Appeals caselaw. Indeed, the claims now specify a very high degree of identity, even higher than that found acceptable in Example 14 of the PTO Written Description Guidelines (relevant pages enclosed). The claim language is also now acceptable under the recent caselaw of the PTO Board of Appeals. We enclose three recent cases that addressed the sequence identity issue, all of which were resolved in favor of the applicant. See *Ex parte Bandman*, 2005 Pat. App. LEXIS 33, Appeal No. 2004-2319 (PTO Bd Pat App Interf 2005); *Ex parte Sun*, 2003 Pat. App. LEXIS 65, Appeal No. 2003-

1993 (PTO Bd Pat App Interf 2003); and *Ex parte Chung*, App. No. 2004-2201 (PTO Bd Pat App Interf 2004).

We have reviewed the various references cited by the Examiner in the enablement section of the action, but the relevance of these documents are unclear in that none appears to concern apo-A-I, or address enablement of the presently claimed invention. It is submitted that in any event, the amendments to the claims now clarify that the invention concerns polypeptide fragments specifically taught or shown in the present specification to correlate with the recited biological function, and to polypeptides having a high degree of sequence identity thereto.

Accordingly, it is submitted that the section 112, first paragraph, concerns have now been appropriately resolved.

IV. Indefiniteness Concerns

It is believed that the concerns under 35 USC 112, second paragraph, with respect to claims 9 and 10 have been fully resolved by the above amendments.

V. Anticipation/Obviousness

The subject Action has rejected all of the claims on the basis of prior art concerns, with the principal reference being US 5,408,038. In reviewing the rejections and the '038 patent, it appears that the Examiner's concern was that the claim scope was uncertain and the claims appeared to read on full-length 267 amino acid long apo-A-I protein, disclosed in Figure 2 and SEQ ID NO:3 of the '038 patent.

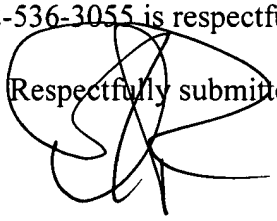
In light of the amendments to the claims with now limit the claims to polypeptides of about 217 amino acids or less or about 182 amino acids or less, or to the specific polypeptide fragments, it is submitted that the '038 patent is no longer relevant.

VI. Conclusion

Applicants believe that the foregoing remarks fully respond to all outstanding matters for this application. Applicants respectfully request that the rejections of all claims be withdrawn so they may pass to issuance.

Should the Examiner desire to sustain any of the rejections discussed in relation to this Response, the courtesy of a telephonic conference between the Examiner, the Examiner's supervisor, and the undersigned attorney at 512-536-3055 is respectfully requested.

Respectfully submitted,



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Date: July 21, 2006

LEXSEE 2005 PAT APP LEXIS 33

Ex parte OLGA BANDMAN, NEIL C. CORLEY, and PURVI SHAH

Appeal No. 2004-2319

Application No. 09/915,694

Board of Patent Appeals and Interferences

2005 Pat. App. LEXIS 33

June 14, 2005, Decided

[*1]

Before WILLIAM F. SMITH, GRIMES, and GREEN, Administrative Patent Judges.

COUNSEL:

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OPINIONBY: GREEN

OPINION:

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

ON BRIEF

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under *35 U.S.C. § 134* from the examiner's final rejection of claims 3, 6, 7, 9 and 12. Claims 3 and 12 are representative of the subject matter on appeal, and read as follows:

3. An isolated polynucleotide encoding a polypeptide selected from the group consisting of:

a) a polypeptide comprising the amino acid sequence of SEQ ID NO: 1; and
b) a polypeptide comprising a naturally occurring amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 1.

12. An isolated polynucleotide selected from the group consisting of:

a) a polynucleotide comprising the polynucleotide sequence of SEQ ID NO: 2,
b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 95% identical to **[*2]** the polynucleotide sequence of SEQ ID NO: 2,
c) a polynucleotide having a sequence complementary to a polynucleotide of a),
d) a polynucleotide having a sequence complementary to a polynucleotide of b) and

e) an RNA equivalent of a)-d).

The examiner relies upon the following references:

Attwood et al. (Attwood), "Which craft is best in bioinformatics?," Computer and Chemistry, Vol. 25, pp. 329-339 (2001)

Ponting, "Issue in predicting protein function from sequence," Briefing in Bioinformatics, Vol. 2, No. 1, pp. 19-29 (2001)

Claims 3, 6, 7, 9 and 12 stand rejected under *35 U.S.C. § 112,* first paragraph, as failing to comply with the written description requirement. In addition, the claims stand rejected under *35 U.S.C. § 112,* first paragraph, as failing to comply with the enablement requirement. After careful review of the record and consideration of the issues before us, we reverse both rejections. We do, however, enter a new ground of rejection under *35 U.S.C. § 112,* second paragraph over claim 12.

DISCUSSION

Written Description

Claims 3, 6, 7, 9 **[*3]** and 12 stand rejected under *35 U.S.C. § 112,* first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

According to the rejection:

The claimed invention encompass[es] [sic] any isolated polynucleotide encoding any polypeptide comprising any naturally occurring amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 1 (claim 3) and any isolated polynucleotide comprising any naturally occurring polynucleotide sequence that is at least 95% identical to the nucleotide sequence of SEQ ID NO: 2 (claim 12).

Examiner's Answer, page 3.

The rejection contends that the specification provides only a single representative species--an isolated polynucleotide consisting of SEQ ID NO: 2. The rejection asserts that "there is no disclosure of any particular structure to function/activity relationship in the single disclosed species." Id. The rejection concludes "given this lack of additional representative species as encompassed **[*4]** by the claims, [appellants] have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize [appellants] were in possession of the claimed invention.

The written description requirement of *35 U.S.C. § 112,* first paragraph, does not require a description of the complete structure of every species within a chemical genus. See *Utter v. Hiraga, 845 F.2d 993, 998,* 6 USPQ2 1709, 1714 (Fed. Cir. 1988) ("A specification may, within the meaning of *35 U.S.C. § 112,* P1, contain a written description of a broadly claimed invention without describing all species the claim encompasses.").

The Court of Appeals for the Federal Circuit, our reviewing court, has addressed the issue of what constitutes adequate written description for a claim drawn to a nucleic acid. In *Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1602 (Fed. Cir. 2002),* the court adopted a portion of the Guidelines proffered by the United States Patent and Trademark Office (USPTO). The court **[*5]** stated that:

> The written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of characteristics.

Enzo Biochem, 296 F.3d at 1324, 63 USPQ2d at 1613 (citations omitted).

In Enzo-Biochem, the court refined the approach advanced by *The Regents of The University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1998),* adopting an example offered in the USPTO guidelines having facts that contrasted with those of Eli Lilly, wherein the written description requirement would be met. Adequate written description may be present for a genus of nucleic acids based on their hybridization properties, "if they hybridize under highly stringent conditions to known sequences because such conditions dictate that all species within the genus will be structurally **[*6]** similar." *Enzo Biochem, 296 F.3d at 1327, 63 USPQ2d at 1615.*

In the case before us, the complete structure of the polynucleotide of SEQ ID NO: 2 has been described, and the genus limited to a polynucleotide comprising a naturally occurring polynucleotide sequence at least 95% identical to the polynucleotide sequence of SEQ ID NO: 2. In addition, the complete structure of the polypeptide of SEQ ID NO: 1 has been described, and the genus limited to polypeptides comprising a naturally occurring amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 1. While the examiner asserts that the specification provides no disclosure of any particular structure to function/activity relationship in the single disclosed species, the examiner has not adequately explained and/or provided evidence to support that assertion. Thus, the rejection of claims 3, 6, 7, 9 and 12 under *35 U.S.C. § 112,* first paragraph, for lack of adequate written description, is reversed.

Enablement

Claims 3, 6, 7, 9 and 12 stand rejected under *35 U.S.C. § 112,* first paragraph, **[*7]** on the grounds that the claims contain subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

According to the rejection:

> The claimed invention encompass[es] [sic] any isolated polynucleotide encoding any polypeptide comprising any naturally occurring amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 1 (claim 3) and any isolated polynucleotide comprising any naturally occurring polynucleotide sequence that is at least 95% identical to the nucleotide sequence of SEQ ID NO: 2 (claim 12).

Examiner's Answer, page 4.

The rejection contends that while the specification provides guidance for an isolated polynucleotide consisting of SEQ ID NO: 2, it "does not teach the specific structural /catalytic amino acids and the structural motifs essential for protein activity/function which cannot be altered." Id. The rejection asserts further that

> The amount of experimentation to make the claimed polynucleotide is enormous and undue and entails selecting specific nucleotides to change (deletion **[*8]** insertion, substitution, or combinations thereof) in any polynucleotide to make a polynucleotide encoding a polypeptide comprising an amino acid sequence that is at least 95% identical to SEQ ID NO: 1 or selecting specific nucleotides to change (deletion, insertion, substitution, or combinations thereof) in the nucleotide sequence of SEQ ID NO: 2 to make a polynucleotide that has a nucleotide sequence that is at least 95% identical to SEQ ID NO: 2 and determining by assays whether the encoded polypeptide has malate dehydrogenase activity.

Id. at 5.

Appellants argue that "independent claim 3 recites not only that the 'variant' polynucleotides encode polypeptides that are at least 95% identical to SEQ ID NO: 1, but also have 'a naturally occurring amino acid sequence.'" Appeal Brief, page 10 (emphasis in original). Thus, appellants contend, "through the process of natural selection, nature will have determined the appropriate amino acid sequences," and given the information provided by SEQ ID NO: 1, the specification enables one skilled in the art to obtain a polynucleotide encoding a polypeptide comprising a naturally-occurring amino acid sequence at least 95% identical **[*9]** to the amino acid sequence of SEQ ID NO: 1. We agree.

The examiner bears the initial burden of showing nonenablement. See *In re Wright, 999 F.2d 1557, 1561-62, 27*

USPQ2d 1510, 1513 (Fed. Cir. 1993). "Enablement requires that the specification teach those in the art to make and use the invention without 'undue experimentation.' . . . That some experimentation may be required is not fatal; the issue is whether the amount of experimentation required is 'undue.'" *In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991)* (emphasis in original). Some experimentation, even a considerable amount, is not "undue" if, e.g., it is merely routine, or if the specification provides a reasonable amount of guidance as to the direction in which the experimentation should proceed. See *In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).*

The examiner argues that "the recitation of 'naturally occurring amino acid sequence' in the claims does not meet the enablement requirement since the specification must still provide guidance regarding **[*10]** the specific amino acid residues in the amino acid sequence of SEQ ID NO: 1 which cannot be changed and amino acid residues which can be changed but still retain malate dehydrogenase." Examiner's Answer, page 14. That argument is not agreed with because the examiner has not explained and/or provided evidence why a naturally occurring polynucleotide sequence that is at least 95% identical to the polynucleotide sequence of SEQ ID NO: 2, or a naturally occurring polypeptide that is at least 95% identical to the amino acid sequence of SEQ ID NO: 1 would not have malate dehydrogenase activity. As explained by appellants, "through the process of natural selection, nature will have determined the appropriate amino acid sequences." Thus, the rejection of claims 3, 6, 7, 9 and 12 under *35 U.S.C. § 112,* first paragraph, for lack of enablement, is reversed.

NEW GROUND OF REJECTION

Under the provisions of 37 CFR § 41.50(b), we enter the following new ground of rejection: Claim 12 is rejected under *35 U.S.C. § 112,* second paragraph, as indefinite. The scope of the claim is indefinite because of its recitation of "a naturally **[*11]** occurring polynucleotide sequence at least 95% identical to the polynucleotide sequence of SEQ ID NO: 2 . . . [and] an RNA equivalent [thereof]."

The normal meaning of "polynucleotide" is a polymer made up of nucleotides. Nucleotides are made up of a purine or pyrimidine base joined to a sugar residue (deoxyribose in DNA, ribose in RNA) and a phosphate group. Thus, according to its normal meaning, part (b) of claim 12 would encompass both DNA and RNA. Read in light of the rest of the claim and the specification, however, the scope of the claim becomes unclear.

First, SEQ ID NO:2 is a DNA sequence since it contains thymine (T) residues. The equivalent RNA sequence would have uracil (U) in place of thymidine. It is unclear, however, whether T and U would be considered to be "identical" residues in computing whether a given polynucleotide was "95% identical" to SEQ ID NO:2.

Second, if part (b) of claim 12 is intended to include both DNA and RNA, then part (e) of the claim is entirely superfluous. That is, there would be no need for a part (e) directed to "RNA equivalent[s]" unless parts (a) through (d) of claim 12 are intended to be limited to DNA, rather than encompassing both DNA and **[*12]** RNA.

These factors suggest that claim 12 uses the term "polynucleotide" as a synonym for DNA, rather than using it in its usual sense of encompassing both DNA and RNA. However, construing part (b) of the claim as limited to DNA presents its own problems. If part (b) of claim 12 were construed to encompass only "naturally occurring [DNA] sequence[s] at least 95% identical to the [DNA] sequence of SEQ ID NO:2", that part of the claim would very likely define a compound that does not exist.

The DNA shown in the specification's SEQ ID NO:2 is a cDNA sequence. See, working examples I, II and III (headed "THP1PLB01 cDNA Library Construction," "Isolation and Sequencing of cDNA Clones," and "Homology Searching of cDNA clones and Their Deduced Proteins," respectively).

cDNA sequences are not naturally occurring. They are laboratory-made DNA copies of naturally occurring messenger RNA (mRNA) sequences. The only naturally occurring DNA sequence that encodes the protein of SEQ ID NO:1 is a genomic sequence. That genomic sequence is then transcribed by the cell into an RNA equivalent that is processed and eventually translated into the polypeptide of SEQ ID NO:1. The processing steps required **[*13]** to generate an mRNA from a genomic DNA include removal of intervening sequences, or introns.

Virtually all human genes include introns. Thus, those skilled in the art would expect that the naturally occurring gene encoding the polypeptide of SEQ ID NO:1 would be interrupted by several introns. As a result, those skilled in the art would expect that, more likely than not, no naturally occurring DNA would be 95% identical to SEQ ID NO:2 because the parts of the naturally occurring gene that are identical to SEQ ID NO:2 would be interrupted by introns that are not part of the cDNA sequence of SEQ ID NO:2.

The naturally occurring gene that encodes the polypeptide of SEQ ID NO:1 would only fall within the scope of part (b) of claim 12 if it has introns that comprise 5% or less of its sequence. If the naturally occurring gene contains greater than 5% introns, it would appear that there is no naturally occurring DNA sequence that is 95% identical to SEQ ID NO:2. Thus, if part (b) of claim 12 is construed as being limited to DNA, it is overwhelmingly likely to be a nullity. It would add nothing to the scope of the claim.

On the other hand, if part (b) of claim 12 were construed to encompass **[*14]** both DNA and RNA, in addition to the ambiguities discussed above it would present issues of enablement that have not been discussed on the record. That is, if the claim encompasses both DNA and RNA, and if the corresponding genomic DNA does not contain an anomalously small amount of intron DNA, the only "naturally occurring" polynucleotides that would be 95% identical to SEQ ID NO:2 would be mRNAs (which are processed to excise introns).

Claim 12 is directed to an "isolated" polynucleotide, but the specification provides no guidance on how to isolate the particular mRNA corresponding to SEQ ID NO:2. Thus, if part (b) of claim 12 is construed to encompass both DNA and RNA, then for the reasons discussed above, the DNA aspect is probably a nullity and it is unclear whether the specification provides adequate guidance to enable those skilled in the art to make and use the mRNA that represents the remainder of the invention defined by part (b).

Finally, even assuming that part (b) of claim 12 were construed to encompass naturally occurring mRNAs that are at least 95% identical to SEQ ID NO:2, and assuming that the specification provides an enabling disclosure for such mRNAs, the scope **[*15]** of the claims would still be unclear. The specification provides no guidance that would allow those skilled in the art to determine, with a reasonable degree of confidence, whether any of the sequences that are at least 95% identical to SEQ ID NO:2 occur naturally and, if so, which they would be. The only way to definitely fix the scope of the claims would be to compare SEQ ID NO:2 to all naturally occurring sequences, clearly an impossible task. Thus, even if we were to ignore the various ambiguities discussed above, the metes and bounds of the claim are unclear.

As the Federal Circuit recently noted,

> the Supreme Court explained the reason underlying the indefiniteness doctrine 60 years ago in *United Carbon Co. v. Binney & Smith Co., 317 U.S. 228, 236, 55 USPQ 381, 385 (1942):*
>
> > A zone of uncertainty which enterprise and experimentation may enter only at the risk of infringement claims would discourage invention only a little less than unequivocal foreclosure of the field. Moreover, the claims must be reasonably clear-cut to enable courts to determine whether novelty and invention are genuine.

Exxon Research and Eng'g Co. v. United States, 265 F.3d 1371, 1376, 60 USPQ2d 1272, 1276 (Fed. Cir. 2001). **[*16]** The court held that compliance with *35 U.S.C. § 112,* second paragraph, is determined by "whether 'the claims at issue [are] sufficiently precise to permit a potential competitor to determine whether or not he is infringing.'" Id. (bracketed text in original, quoting *Morton Int'l, Inc. v. Cardinal Chem. Co., 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993)).* That test is not met here.

For all these reasons, the scope of claim 12 is unclear. The test for definiteness is "whether one skilled in the art would understand the bounds of the claim when read in light of the specification." *Miles Laboratories Inc. v. Shandon Inc., 997 F.2d 870, 875, 27 USPQ2d 1123, 1126 (Fed. Cir. 1993).* See also *Amgen, Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1342, 65 USPQ2d 1385, 1406 (Fed. Cir. 2003):* "Ambiguity in claim scope is at the heart of the definiteness requirement of *35 U.S.C. § 112,* P2." Since we cannot determine the scope of claim 12, we conclude that it is indefinite. **[*17]** Claim 12 is rejected under *35 U.S.C. § 112,* second paragraph.

TIME PERIOD FOR RESPONSE

This decision contains a new ground of rejection pursuant to 37 CFR § 41.50(b) (effective September 13, 2004, *69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21* (September 7, 2004)). 37 CFR § 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review."

37 CFR § 41.50(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

> (1) *Reopen prosecution.* Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner. . . .
>
> (2) *Request rehearing.* Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .

No time period for taking any subsequent action **[*18]** in connection with this appeal may be extended under 37 CFR § 1.136(a).

REVERSED, 37 CFR § 41.50(b)

LEXSEE 2003 PAT APP LEXIS 65

Ex parte YUEJIN SUN, BRIAN R. DILKES, BRIAN A. LARKINS, KEITH S. LOWE, WILLIAM J. GORDON-KAMM and RICARDO A. DANTE

Appeal No. 2003-1993

Application No. 09/470,526

Board of Patent Appeals and Interferences

2003 Pat. App. LEXIS 65

February 27, 2003, Decided

[*1]

Before WILLIAM F. SMITH, MILLS and GRIMES, Administrative Patent Judges.

OPINIONBY: MILLS

OPINION:

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

ON BRIEF

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under *35 U.S.C. § 134* from the examiner's final rejection of claims 2-11, 31, 33 and 35-36 which are the claims on appeal in this application. Claims 14, 32 and 37 have been allowed.

Claim 31 is illustrative of the claims on appeal and reads as follows:

31. An isolated wee1 nucleic acid comprising a member selected from the group consisting of:
(a) a polynucleotide that encodes a polypeptide of SEQ ID NO:2.;
(b) a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1;
(c) a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1; and
(d) a polynucleotide complementary to a polynucleotide of (a) through (c).

The prior art references relied upon by the examiner are:

Aligue et al. (Aligue), "Regulation of *Schizosaccharomyces pombe* Wee1 Tyrosine Kinase," J. Biol. Chem., **[*2]** Vol. 272, pp. 13320-13325 (1997)

Hemerly et al. (Hemerly), "Dominant negative mutants of the Cdc2 kinase uncouple cell division from iterative plant development," The EMBO Journal, Vol. 14, pp. 3925-3936 (1995)

Grounds of Rejection

Claims 2-11, 31, 33 and 35-36 stand rejected under *35 U.S.C. § 112,* first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention.

Claims 2-11, 31, 33 and 35-36 stand rejected under *35 U.S.C. § 112,* first paragraph for lack of enablement.

These rejections are reversed.

DISCUSSION

In reaching our decision in this appeal, we have given consideration to the appellants' specification and claims, to the applied references, and to the respective positions articulated by the appellants and the examiner.

Rather than reiterate the conflicting viewpoints advanced by the examiner and the appellants regarding the noted rejections, we make reference to the examiner's Answer for the examiner's reasoning **[*3]** in support of the rejection, and to the appellants' Brief for the appellants' arguments thereagainst. As a consequence of our review, we make the determinations which follow.

Background

The subject matter of the present application is generally directed to corn plant nucleic acids and their encoded proteins which are involved in cell cycle regulation. Specification, page 4. In particular, the claimed invention is directed to a wee1 homologue from maize, zmwee1, whose activity resembles related protein tyrosine kinases. Specification, page 6. The zmwee1 protein is indicated in the specification to be useful in the genetic engineering of the corn plant to increase maize productivity. Specification, page 3.

More specifically, claim 31 is directed to an isolated wee1 nucleic acid comprising a member selected from the group consisting of: a polynucleotide that encodes a polypeptide of SEQ ID NO:2.; a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1; a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1; and a polynucleotide complementary to a polynucleotide described above.

According to the prior art, Aligue, Wee1 tyrosine **[*4]** kinase regulates mitosis by carrying out the inhibitory tyrosine 15 phosphorylation of Cdc2 M-phase inducing kinase. Abstract. The specification confirms this, stating "induced wee1 overexpression results in phosphorylation of p34 at tyrosine-15 (inactivating p34), effectively blocking the transition from G2 into mitosis." Specification, page 37. The "encoded [wee1] protein is an important part of the checkpoint control machinery that regulates p34<cdc2> activity and it's [sic] participation in the active MPF (maturation promoting factor) complex." Specification, page 36. Wee1 activity can be stimulated by the CDK2-cyclin A complex, or inhibited by nim1. Specification, page 36.

Description

Claims 2-11, 31, 33 and 35-36 stand rejected under *35 U.S.C. § 112,* first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention.

The Federal Circuit has discussed the application of the written description requirement of the first paragraph of § 112 to inventions in the **[*5]** field of biotechnology. See *University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).* The court explained that

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus . . . However, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously **[*6]** indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id.

The Lilly court also stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Id. at 1567, 43 USPQ2d at 1405.* Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id. at 1568, 43 USPQ2d at 1406.*

The Federal Circuit has also addressed the written description requirement in the context of DNA-related inventions. See *Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002).* **[*7]** The Enzo court adopted the standard that "the written description requirement can be met by 'showing that an invention is complete by disclosure of **sufficiently detailed, relevant identifying characteristics** . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" [Emphasis added] *Id. at 1324, 63 USPQ2d at 1613.*

The court in Enzo adopted its standard from the USPTO's Written Description Examination Guidelines. See *296 F.3d at 1324, 63 USPQ2d at 1613* (citing the Guidelines). The Guidelines apply to proteins as well as DNAs.

Finally, it is well-settled that the written description requirement of *35 U.S.C. § 112,* first paragraph, can be satisfied without express or explicit disclosure of a later-claimed invention. See, e.g., *In re Herschler, 591 F.2d 693, 700, 200 USPQ 711, 717 (CCPA 1979):* "The claimed subject matter **[*8]** need not be described in haec verba to satisfy the description requirement. It is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants invented processes including those limitations." (citations omitted). See also *Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000)* ("In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide in haec verba support for the claimed subject matter at issue.").

We apply the relevant law above to the facts before us. In the present case, the examiner argues that the "specification does not set forth what specific structural or physical features define the claimed isolated nucleic acids and transgenic cells, plants and seeds." Answer, page 4. The examiner argues that one skilled in the art "could not predict the structure and function of isolated nucleic acids comprising a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID **[*9]** NO:1 or a polynucleotide complementary thereto, or cells, plants and seeds transformed therewith. The physical features of the claimed isolated nucleic acids and transgenic cells, plants, and seeds cannot be ascertained in the absence of information about the functional activities of these nucleic acids. Additionally, the specification does not disclose the effect of incorporating the claimed isolated nucleic acids into the genome of a cell or plant." Id.

We find the examiner's argument that one skilled in the art could not predict the structure and function of isolated nucleic acids comprising a wee1 to be confusing in the context of a written description rejection, as predictability is not the legal standard or test for such rejections. However, as best we can understand the examiner's argument, the examiner appears to argue that the specification does not describe a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1.

The examiner argues that "Applicant's [sic] own specification fails to teach a single representative species with 80% identity and WEE1 function." Answer, page 5.

We do not agree with the examiner that claim 31 lacks **[*10]** written description in the specification and that appellants were not in possession of the claimed invention at the time the application was filed. First, to satisfy the written description requirement it is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants invented the claimed subject matter. Thus, we do not find the fact that the specification does not specifically teach the structure of a species with 80% identity and WEE1 function to be dispositive of the written description issue here.

The Enzo court stated that "the written description requirement can be met by 'showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" *Id. at 1324, 63 USPQ2d at*

1613 (emphasis omitted, bracketed material **[*11]** in original).

The specification specifically describes the chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1. The specification also provides an example of how to screen for WEE1 activity, specification, Example 1, pages 33-34 and Example 3. Contrary to the examiner's position, it would reasonably appear that such a description in the specification would constitute sufficiently detailed, relevant identifying characteristics of the claimed subject matter consistent with *Enzo (supra).*

In our view, the examiner has failed to indicate why one of ordinary skill in the art, who is in possession of the very specific chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, would be unable to recognize, upon reading the disclosure, that appellants invented the claimed subject matter, including homologues sharing structural features with the specifically claimed and disclosed structures.

The examiner relies on Aligue for the teaching **[*12]** that amino acids 363-408 of the 550 amino acid N-terminal regulatory domain of *S. pombe* WEE1 are critical to the function of the regulatory domain. The examiner concludes that because "the functional properties of WEE1 and other proteins reside in specific amino acid residues, changes in these residues could have an effect on WEE1 function." Answer, page 5.

We agree with appellants that the examiner has not established with a preponderance of the evidence, that the combination of the disclosure of the specific chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, as well as teachings in the specification on how to test for wee1 activity and teachings of the areas of the wee1 gene that can be altered without disturbing substrate recognition are insufficient to describe a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. What is evident from the record is those of ordinary skill in the art were aware that most of the variations in amino acid sequences of WEE1 are in the amino terminus, while the carboxy end of the genes are relatively conserved. Those of skill in the art were also aware that the **[*13]** carboxyl terminus and the central portion of the WEE1 protein from *S. pombe* contain the protein kinase domains and sequence crucial for substrate recognition and catalysis. Thus, those of ordinary skill in the art would have recognized from reading the disclosure that the inventors had invented the isolated wee1 having the specific nucleotide and amino acid sequences and variations of these sequences with mutations in described specific areas of Wee1, while avoiding the introduction of mutations in other regions. This teaching, coupled with the ability to test for functional mutants with the assays provided for in the specification, supports appellants' position that the inventors sufficiently described and were in possession of the invention as claimed, at the time of filing of the patent application.

In our view the examiner has not provided sufficient evidence or analysis to indicate why one of ordinary skill in the art having read the disclosure, would not have been able to recognize that the inventors invented the subject matter within the scope of the claims. The rejection of the claims for lack of written description is reversed.

Enablement

Claims 2-11, 31, 33 and **[*14]** 35-36 stand rejected under *35 U.S.C. § 112,* first paragraph for lack of enablement.

It is the examiner's position that the specification is enabling for an isolated wee1 nucleic acid comprising a polynucleotide encoding SEQ ID NO:2 and a polynucleotide comprising SEQ ID NO:1, but does not reasonably provide enablement for a wee1 polynucleotide having 80% identity to the coding region of SEQ ID NO:1. Answer, page 6.

Enablement is a legal determination of whether a patent enables one skilled in the art to make and use the claimed invention, *Raytheon Co. v. Roper Corp., 724 F.2d 951, 960, 220 USPQ 592, 599 (Fed. Cir. 1983),* and is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly extensive. *Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984); W.L. Gore and Associates v. Garlock, Inc., 721 F.2d 1540, 1556, 220 USPQ 303, 315 (Fed. Cir. 1983).* Nothing more than objective enablement is required, **[*15]** and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples. *In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971).*

An analysis of whether the claims under appeal are supported by an enabling disclosure requires a determination of

whether that disclosure contained sufficient information regarding the subject matter of the appealed claims as to enable one skilled in the pertinent art to make and use the claimed invention. In order to establish a prima facie case of lack of enablement, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. See *In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)* (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). See also *In re Morehouse, 545 F.2d 162, 192 USPQ 29 (CCPA 1976).*

The threshold step in resolving this issue is to determine whether the examiner **[*16]** has met his burden of proof by advancing acceptable reasoning inconsistent with enablement. "Factors to be considered by the examiner in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman, [230 USPQ 546, 547 (Bd Pat App Int 1986)].* They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." (footnote omitted). *In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404,* (Fed. Cir. 1988).

In the present case the examiner provided an analysis of several of the relevant enablement factors on pages 5-9 of the Answer. One of the examiner's primary arguments is that the specification does not disclose any specific structural or functional characteristics of any isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding **[*17]** region of SEQ ID NO:1. Answer, page 7. The examiner also argues that the "specification does not disclose any examples of how to make a transgenic host cell or plant comprising an isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1" or provide "any definitive evidence that introducing any isolated nucleic acid comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 into a plant will result in an alteration of the plant's phenotype." Id.

The examiner relies on Hemerly to support the position that the transformation of plant material is unpredictable in view of the disclosure. According to the examiner, Hemerly teaches "the transformation of *Arabidopsis* and tobacco plants with isolated nucleic acids encoding wild-type and mutant Cdc2a cell cycle regulatory proteins". Answer, page 8. Transformation of *Arabidopsis* with wild-type Cdc2a and with a Cdc2a mutant designed to accelerate the cell cycle unexpectedly did not affect the development of transgenic plants. The transformation of *Arabidopsis* and tobacco with a Cdc2a mutant designed to arrest the cell cycle **[*18]** did affect the development of transgenic plants as expected. Id.

The examiner concludes (Id., pages 8-9)

> Given the unpredictability of determining the function of isolated nucleic acids comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1, the unpredictability of altering the phenotype of a plant by transforming it with an isolated nucleic acid of SEQ ID NO:1 or isolated nucleic acids comprising a polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1, the absence of guidance in the specification for making and using said nucleic acids and transgenic host cells, plants, and seeds, the lack of working examples, and given the breadth of the claims which encompass multiple polynucleotides having at least 80% identity to the entire coding region of SEQ ID NO:1, it would require undue experimentation by one skilled in the art to make and/or use the claimed invention.

Analysis of the enablement requirement in the present case dovetails with our analysis with respect to the written description requirement. In particular, the specification specifically describes the chemical structures of a polynucleotide **[*19]** that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1. The specification also provides an example of how to screen for WEE1 activity, specification, Example 1, pages 33-34 and Example 3. Brief, page 9. In addition, the specification page 3, lines 17-31, "describes the level of skill in the art as well as indicating areas of the wee1 gene that can be altered without disturbing substrate recognition." Brief, page 7. Moreover, the specification, page 3, states, "Most of the variations in amino acid sequences of WEE1 are in the amino terminus, while the carboxy end of the genes are relatively conserved. The carboxyl terminus and the central portion of the WEE1 protein from *S. pombe* contain the protein kinase domains and sequence crucial for substrate recognition and catalysis."

We agree with appellants that the examiner has not established that the combination of the disclosure of the

specific chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1, as well as teachings in the specification on how to test for wee1 activity and teachings of the areas of the wee1 gene that can be **[*20]** altered without disturbing substrate recognition are insufficient to enable a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1.

Nor has the examiner established that one of ordinary skill in the art having the chemical structures of a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1 and the ability to test for expression as described in the specification, would be insufficient to transform cells, plants and seeds in view of the success described in the specification. While the examiner relies on Hemerly for the transformation of *Arabidopsis* with wild-type Cdc2a and with a Cdc2a mutant, the examiner has not explained how or why potential unpredictability associated with Cdc2a expression is related to or affects Wee1 expression. Nor is it clear from the examiner's analysis that the examiner has fully considered the state of the art as it relates to the transformation of vectors, seeds and plant cells, as outlined in the specification.

The Patent and Trademark Office Board of Appeals stated:

> The test [for enablement] is not merely quantitative, since a considerable amount of experimentation is permissible, if it **[*21]** is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

Ex parte Jackson, 217 USPQ 804, 807 (1982).

In our view, upon reading the disclosure, those of ordinary skill in the art would have been provided a reasonable amount of guidance to make and use a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1. The specification, pages 27-29 outlines methods for transfection and transformation of cells and the introduction of DNA into plants. The examples of the specification indicate successful expression of zmwee1 in E. coli as evidenced by the successful inhibition of cyclin-dependent protein kinase. Specification, pages 33-34. In view of the successful transformation of cells with the disclosed and claimed specific wee1, we find no evidence or sufficient indicated reason of record why one of ordinary skill in the art would not have had a reasonable expectation of success in transforming cells and plant cells **[*22]** with a wee1 polynucleotide having at least 80% identity to the entire coding region of SEQ ID NO:1 without undue experimentation.

The rejection of the claims for lack of enablement is reversed.

CONCLUSION

The rejection of claims 2-11, 31, 33 and 35-36 under *35 U.S.C. § 112,* first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art at the time the application was filed that the inventor had possession of the claimed invention is reversed.

The rejection of claims 2-11, 31, 33 and 35-36 under *35 U.S.C. § 112,* first paragraph for lack of enablement is reversed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

REVERSED

2005 WL 191060 (Bd.Pat.App & Interf.)

(Cite as: 2005 WL 191060 (Bd.Pat.App & Interf.))

*1 THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

Board of Patent Appeals and Interferences

Patent and Trademark Office (P.T.O.)

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Appeal No. 2004-2201

Application No. 09/788,476

NO DATE REFERENCE AVAILABLE FOR THIS DOCUMENT

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WILLIAM F. SMITH, MILLS, and GRIMES

Administrative Patent Judges

WILLIAM F. SMITH

Administrative Patent Judge

ON BRIEF [FN1]

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the examiner's refusal to allow claim 1. Claims 15-17 are stated by appellants to have been indicated allowable by the examiner. Appeal Brief received December 10, 2003, page 2.

1. An isolated nucleic acid comprising the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3 or a nucleotide sequence, having at least about 60% similarity to the full length of SEQ ID NO:1 or SEQ ID NO:3, that hybridizes to SEQ ID NO:1 or SEQ ID NO:3 under conditions of 0.1 x SSC buffer, 0.1% w/v SDS, at a temperature of at least 65° C, wherein an mRNA corresponding to said nucleic acid is differentially or preferentially expressed in human hepatocellular carcinoma tissue or tissue from pancreatic adenocarcinoma relative to other tissue in said subject and/or in subjects not diagnosed with this condition.

Claim 1 stands rejected under 35 U.S.C. § 112, first paragraph (written description and enablement). The examiner does not rely upon any evidence in

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support of these rejections. We reverse.

Background

Appellants discuss the present invention at page 21 of the specification as follows:

> The present invention is described hereinafter with reference to the detection of one particular gene designated hcc-1 from the human hepatocellular carcinoma cell line, HCC-M. The nucleotide sequence of hcc-1 is provided in SEQ ID NO:1. The corresponding expression product is a protein designated HCC-1 and this comprises an amino acid as set forth in SEQ ID NO:2. A PCR extended form for use in a vector is shown in SEQ ID NO:3.

As seen, claim 1 is directed to an isolated nucleic acid comprising the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3. In addition, claim 1 comprises a nucleotide sequence having at least about 60% similarity to the full length of SEQ ID NO:1 or SEQ ID NO:3 that hybridizes to SEQ ID NO:1 or SEQ ID NO:3 under specified conditions. In addition, the third nucleotide sequence encompassed by claim 1 is required to have an mRNA that corresponds thereto that is differentially or preferentially expressed in human hepatocellular carcinoma tissue or tissue from pancreatic adenocarcinoma relative to other tissue in the subject and/or in subjects not diagnosed with this condition.

Discussion

1. Written Description.

*2 The Federal Circuit discussed the application of the written description requirement to inventions in the field of biotechnology in University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), stating that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. at 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. at 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be

described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

Both appellants and the examiner believe that the written description issue raised in this rejection is similar to the issue raised in Example 9 of the training materials issued in conjunction with the USPTO written description guidelines. See, "Synopsis of Application of Written Description Guidelines," at 35, available at http://www.uspto.gov/web/menu/written.pdf. The hypothetical claim which is the subject of Example 9 of the Guidelines reads as:

an isolated nucleic acid that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO:1, wherein said nucleic acid encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity.

*3 We first note that the hybridization conditions set forth in claim 1 on appeal are stated to be "high stringency." Specification, page 25, lines 3-4. The examiner's reasoning as to why the present fact situation is not analogous to that set forth in Example 9 of the Guidelines is as follows:

In the hypothetical claim 1 of Example 9 in the Guidelines, the structure of the claimed genus encodes a protein with the recited function. In other words, the recited function is dictated by the chemical structure of the claimed genus.

However, unlike the situation in Example 9 of the Guidelines, the instantly recited function is not associated with the structural feature of claimed genera, but associated with human disease status. In the instant claim 1, the recited function is not dictated by chemical structure of the claimed genus but dictated by other events i.e. that pancreatic adenocarcinoma or HCC is developed in a host. In other words, the expression is not function associated with the structure but a reaction of a human body to certain stimuli, in the instant case the development of HCC or pancreatic adenocarcinoma.

In summary, the functional characteristic recited is uncoupled with the structure of the claimed genus. There is no correlation between the chemical structure of the claimed genus and the recited function. Therefore the recited functional language describing the claimed genera does not adequately describe the common feature of claimed generic nucleic acid molecule.

Examiner's Answer, pages 8 and 9.

The analysis of the reasoning set forth in Example 9 of the Guidelines as to why hypothetical claim 1 of that example complies with the written description requirement is as follows:

Now turning to the genus analysis, a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs. Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill in the art are adequate to determine that applicant was in possession of the claimed invention.

Guidelines at 36-37.

We disagree with the examiner's analysis that claim 1 on appeal does not comply with the written description requirement because the expression of the claimed nucleic acid is "not function associated with the structure but a reaction of the human body to certain stimuli, in the instant case the development of HCC or pancreatic adenocarcinoma." Example 9 of the Guidelines does not place any restriction as to how the coding function of the DNA may be claimed. A determination whether a given nucleic acid is within the scope of the hypothetical claim of Example 9 of the Guidelines would require expressing the nucleic acid and testing the protein to determine whether it binds to a dopamine receptor and stimulates adenylate cyclase activity. A determination whether a given nucleic acid is within the scope of claim 1 would also require testing, albeit different testing. According to the terms of claim 1, an mRNA corresponding to the nucleic acid must be differentially or preferentially expressed in human hepatocellular carcinoma tissue or tissue from pancreatic adenocarcinoma relative to other tissue in said subject and/or in subjects not diagnosed with this condition. The examiner states that the functional characteristic recited in claim 1 is "uncoupled with the structure of the claim genus," Examiner's Answer, page 9, but does not explain why that is significant in determining whether claim 1 complies with the written description analysis. The training materials are not the end-all of a written description analysis. The fact that a given claim under review does not fit squarely within one of the examples does not mean that that claim does not comply with the written description requirement. Rather than merely pointing out that claim 1 differs from the hypothetical claim in Example 9 of the Guidelines, an analysis is needed from the examiner explaining why the function set forth in claim 1 is not an adequate identifier of the claimed genus of nucleic acids. Instead, all we have is the examiner's conclusion that claim 1 on appeal is different from the hypothetical claim of Example 9 of the Guidelines and therefore claim 1 on appeal does not comply with the written description requirement. This is insufficient.

*4 The examiner's rejection under 35 U.S.C. § 112, first paragraph (written description), is reversed.

2. Enablement.

In stating the rejection on pages 5-6 of the Examiner's Answer, the examiner has focused on the purported need to screen a "large quantity of clinical samples" in order to enable claim 1 throughout its scope. In reviewing the examiner's response to arguments in regard to this rejection on pages 10-13 of the Examiner's Answer we find the examiner again focuses on the need to screen "a large quantity of clinical samples." Id., page 10. As stated at page 11 of the Examiner's Answer, "in order to make the full scope of the invention, one skilled in the art has to screen a large quantity of clinical samples from liver or pancreatic tissue of patients having HCC or pancreatic adenocarcinoma, followed by sequence [sic] the nucleic acid composition."

As set forth in PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996):

In unpredictable art areas, this court has refused to find broad generic claims enabled by specifications that demonstrate the enablement of only one or a

few embodiments and do not demonstrate with reasonable specificity how to make and use other potential embodiments across the full scope of the claim. See, e.g., In re Goodman, 11 F.3d 1046, 1050-52, 29 USPQ2d 2010, 2013-15 (Fed. Cir. 1993); Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d. 1200, 1212-14, 18 USPQ2d 1016, 1026-28 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991); In re Vaeck, 947 F.2d at 496, 20 USPQ2d at 1445. Enablement is lacking in those cases, the court has explained, because the undescribed embodiments cannot be made, based on the disclosure in the specification, without undue experimentation. But the question of undue experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation 'must not be unduly extensive.' Atlas Powder Co., v. E.I. DuPont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984). The Patent and Trademark Office Board of Appeals summarized the point well when it stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

***5** Ex parte Jackson, 217 USPQ 804, 807 (1982).

What is missing is an analysis from the examiner as to why the amount of work required to practice the invention of claim 1 throughout its scope would be considered undue instead of routine. It is insufficient for an examiner to merely point out that it is necessary to "screen a large quantity of clinical samples." Examiner's Answer, page 11.

Accordingly, the examiner's rejection under 35 U.S.C. § 112, first paragraph (enablement) is reversed.

The decision of the examiner is reversed.

REVERSED

BOARD OF PATENT APPEALS AND INTERFERENCES

William F. Smith

Administrative Patent Judge

Demetra J. Mills

Administrative Patent Judge

Eric Grimes

Administrative Patent Judge

FN1. We note that a request for oral hearing was made on pages 5-6 of the Reply Brief. Requesting oral hearing in a Reply Brief did not comply with the then

2005 WL 191060 (Bd.Pat.App & Interf.)

(Cite as: 2005 WL 191060 (Bd.Pat.App & Interf.))

existing provisions of 37 CFR § 1.194(b)("If appellant desires an oral hearing, appellant must file, in a separate paper, a written request for such hearing ...."). In view of our disposition of the appeal, appellants' request for oral hearing is moot.

2005 WL 191060 (Bd.Pat.App & Interf.)

END OF DOCUMENT

Example 14: Product by Function

Specification: The specification exemplifies a protein isolated from liver that catalyzes the reaction of A ⟶ B. The isolated protein was sequenced and was determined to have the sequence as set forth in SEQ ID NO: 3. The specification also contemplates but does not exemplify variants of the protein wherein the variant can have any or all of the following: substitutions, deletions, insertions and additions. The specification indicates that procedures for making proteins with substitutions, deletions, insertions and additions is routine in the art and provides an assay for detecting the catalytic activity of the protein.

Claim:

A protein having SEQ ID NO: 3 and variants thereof that are at least 95% identical to SEQ ID NO: 3 and catalyze the reaction of A ⟶ B.

Analysis:

A review of the full content of the specification indicates that a protein having SEQ ID NO: 3 or variants having 95% identity to SEQ ID NO: 3 and having catalytic activity are essential to the operation of the claimed invention. The procedures for making variants of SEQ ID NO: 3 are conventional in the art and an assay is described which will identify other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO: 3 which have 95% identity to SEQ ID NO: 3 and retain its activity are conventional in the art.

A review of the claim indicates that variants of SEQ ID NO: 3 include but are not limited to those variants of SEQ ID NO: 3 with substitutions, deletions, insertions and additions; but all variants must possess the specified catalytic activity and must have at least 95% identity to the SEQ ID NO: 3. Additionally, the claim is drawn to a protein which **comprises** SEQ ID NO: 3 or a variant thereof that has 95% identity to SEQ ID NO: 3. In other words, the protein claimed may be larger than SEQ ID NO: 3 or its variant with 95% identity to SEQ ID NO: 3. It should be noted that "having" is open language, equivalent to "comprising".

The claim has two different generic embodiments, the first being a protein which comprises SEQ ID NO: 3 and the second being variants of SEQ ID NO: 3. There is a single species disclosed, that species being SEQ ID NO: 3.

A search of the prior art indicates that SEQ ID NO: 3 is novel and unobvious.

There is actual reduction to practice of the single disclosed species. The specification indicates that the genus of proteins that must be variants of SEQ ID NO: 3 does not have substantial variation since all of the variants must possess the specified catalytic activity and must have at least 95% identity to the reference sequence, SEQ ID NO: 3. The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity. One of skill in the art would conclude that

applicant was in possession of the necessary common attributes possessed by the members of the genus.

Conclusion: The disclosure meets the requirements of 35 USC §112 first paragraph as providing adequate written description for the claimed invention.

United States Court of Appeals for the Federal Circuit

05-1324
(Interference No. 105,187)

FALKO-GUNTER FALKNER, GEORG HOLZER, and FRIEDRICH DORNER,

Appellants,

v.

STEPHEN C. INGLIS, MICHAEL E.G. BOURSNELL, and ANTHONY C. MINSON,

Appellees.

John P. Isacson, Heller Ehrman LLP, of Washington, DC, argued for appellants. With him on the brief was Paul M. Booth.

Robert G. McMorrow, Jr., Connolly Bove Lodge & Hutz LLP, of Wilmington, Delaware, argued for appellee.

Appealed from: United States Patent and Trademark Office, Board of Patent Appeals and Interferences

United States Court of Appeals for the Federal Circuit

05-1324
(Interference No. 105,187)

FALKO-GUNTER FALKNER, GEORG HOLZER, and FRIEDRICH DORNER,

Appellants,

v.

STEPHEN C. INGLIS, MICHAEL E.G. BOURSNELL, and ANTHONY C. MINSON,

Appellees.

DECIDED: May 26, 2006

Before GAJARSA, Circuit Judge, ARCHER, Senior Circuit Judge and DYK, Circuit Judge.

GAJARSA, Circuit Judge.

This is an appeal from a decision of the Board of Patent Appeals and Interferences ("Board") in Interference No. 105,187, declared on December 24, 2003, between Falkner *et al.*, U.S. Patent No. 5,770,212 ("the Falkner '212 patent") and Inglis *et al.*, U.S. Application Serial No. 08/459,040 ("the Inglis '040 application"). The Administrative Patent Judge (APJ) designated Inglis as the senior party. On December 29, 2004, the Board issued a final decision, holding that Falkner could not antedate Inglis' September 25, 1990 priority date, and entered judgment against Falkner on the

sole count of the interference. It ordered that Falkner was not entitled to claims 1-19 of the Falkner '212 patent. It further ordered that Inglis was entitled to claims 9, 10, 29 and 30 of the '040 application. Falkner filed a timely notice of appeal. This Court has jurisdiction pursuant to 28 U.S.C. § 1295(a)(4)(A) and 35 U.S.C. §§ 141 and 142. For the reasons discussed below, we affirm the judgment of the Board.

I. BACKGROUND

A. The Invention

Some vaccines against a virus (the "target virus") incorporate harmless fragments of the target virus's genetic material into a second virus, called a "viral vector." When a person is vaccinated, the viral vector produces harmless fragments of the target virus, ultimately conferring immunity against it. To prevent the viral vector from itself causing a harmful infection in the inoculee, it must be attenuated. Attenuation is achieved by deleting or inactivating one or more genes responsible for the vector's growth and infectiousness. However, because the vaccine is produced by essentially "growing" the vector virus (accompanied by its inserted target virus gene), attenuation makes it difficult to manufacture the vaccine. The traditional solution to this problem has been to inactivate genes known as "inessential" genes. With inessential genes inactivated, the viral vector is substantially less pathogenic. At the same time, because the vector virus can still fully reproduce itself, albeit more slowly, the vaccine can be produced in commercial quantities. However, the traditional approach carried a disadvantage, namely the risk that the vector virus, though attenuated, could still cause a harmful infection in the inoculee.

The inventors discovered a way of making vaccines safer by deleting or inactivating an essential, rather than an inessential, gene from the viral vector's genome, while at the same time solving the production problem by growing the vaccines in cells that were complementarily modified to produce the absent essential viral gene product "on behalf of" the vector virus. Thus, the modified vector virus could be readily grown in these complementarily-modified cells, but not in other cells, such as those of an inoculee.

This approach is applicable to many different kinds of vector viruses, e.g., adenoviruses, herpesviruses, poxviruses and retroviruses. The subject matter of this interference, however, is directed specifically to vaccines in which the vector virus is a poxvirus. For many vector viruses, there is a risk that vectors that have been attenuated in essential genes can "swap" genes with the host cell genome, thereby reacquiring their deleted genes and reverting to wild-type virus. This risk can be minimized through the use of viruses that are "cytoplasmic", meaning that they are unlikely to enter the cell nucleus. Because a cell's genes are located in the nucleus, cytoplasmic viruses such as poxvirus cannot swap genes with the cell genome and possibly revert to a virulent wild-type virus.

B. Defining the Count and Assigning Priority

The sole count of the interference was either "[a] vaccine according to Claim 1 of Falkner's 5,770,212 patent or a vaccine according to Claim 29 of Inglis' 08/459,040 application." Claim 29 of the Inglis '040 application reads:

> A vaccine comprising a pharmaceutically acceptable excipient and an effective immunizing amount of a mutant virus, wherein said mutant virus is a mutant poxvirus and has a genome which has an inactivating mutation in a viral gene, said viral gene being essential for the production of

> infectious new virus particles, wherein said mutant virus is able to cause production of infectious new virus particles in a complementing host cell gene expressing a gene which complements said essential viral gene, but is unable to cause production of infectious new virus particles when said mutant virus infects a host cell other than a complementing host cell; for prophylactic or therapeutic use in generating an immune response in a subject.

(emphasis added)

Claim 1 of the Falkner '212 patent reads:

> A vaccine comprising (a) a defective poxvirus that lacks a function imparted by an essential region of its parental poxvirus, wherein (i) said defective poxvirus comprises a DNA polynucleotide encoding an antigen and said DNA polynucleotide is under transcriptional control of a promoter, and (ii) the function can be complemented by a complementing source; and (b) a pharmaceutically acceptable carrier.

The Administrative Patent Judge (APJ) designated claims 1-19 of the Falkner '212 patent and claims 9,10, 29, and 30 of the Inglis '040 application as corresponding to the interference count.[1] Both parties sought the benefit of earlier-filed applications to establish dates of constructive reduction to practice.[2] The ALJ accorded the Inglis '040

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[1] Inglis's claim 29 is his broadest claim, directed to poxvirus; and claim 30, which depends on claim 29, is a poxvirus vaccine for mammalian subjects. Claim 9 is directed to poxvirus but contains some additional limitations unrelated to the type of virus used; claim 10 depends on claim 9 and is directed to a single species of poxvirus, namely vaccinia virus. Falkner's claims 2-10 depend on claim 1. Falkner claim 10 is directed to a method of producing the vaccine of claim 1, and the remaining method claims depend thereon.

[2] Priority in an interference goes to the first to invent, but a rebuttable presumption exists that the inventors made their inventions in the chronological order of their effective filing dates, namely that the senior party invented first, see 37 C.F.R. § 1.657(a) (2004), and the junior party bears the burden of proving otherwise, see § 1.657(b), such as by proving that she actually reduced the invention to practice before the constructive filing date (priority date) of the senior party, or that she was first to conceive and diligently reduced the invention to practice, starting from a date prior to reduction to practice by the senior party. See 35 U.S.C. § 112(g) (2000). Falkner sought to rely, in part, on an alleged date of conception and beginning of reasonable diligence: April 27, 1994.

application (filed June 2, 1995) the benefit of several earlier-filed applications, dating back to September 25, 1990.[3] Likewise, the APJ accorded the Falkner '212 patent (issued June 23, 1998 from an application filed February 21, 1997) the benefit of earlier-filed applications, but these dated back only to April 29, 1994.[4] Consequently, the APJ designated Inglis as the senior party.

C. Board Decision

The specifications of all of Inglis' earlier applications were similar. Although they focused on herpesvirus vectors, they contained several passages related to poxvirus-based vaccines. Because Falkner believed that these passages did not adequately describe and enable the poxvirus invention, he challenged both Inglis' entitlement to priority as to the count and the patentability of Inglis' corresponding claims. Falkner brought these challenges in three closely-related preliminary motions before the Board.

On September 13, 2004, the "600" rules expired in favor of new rules found at 37 C.F.R. § 41.100 et seq. However, the Board correctly chose to decide the matter under the old rules, given the parties' reliance on them in filing all motions, oppositions, and replies in the case, which were completed before the new rules took effect. See Singh v. Brake, 222 F.3d 1362, 1371 (Fed. Cir. 2000) (applying a new procedural rule if and only if it did not affect the parties' reliance interests).

[3] The Inglis priority applications were U.S. Application Serial No. 08/384,963 ("the Inglis '963 application"), filed February 7, 1995; U.S. Application Serial No. 08/030,073 ("the Inglis '073 application"), filed May 20, 1993; WO/92/05263, PCT/GB91/01632 ("the Inglis PCT application"), filed September 23, 1991, published in English on April 2, 1992; GB 9104903.1 ("the Inglis 1991 British application"), filed March 8, 1991; and GB 9020799.4 ("the Inglis 1990 British application"), filed September 25, 1990. The Inglis '040 application is a continuation in part of the '963 application, which was in turn a continuation of the Inglis '073 application. The '073 application corresponded to the Inglis PCT application. The Inglis PCT application claimed priority to, and was essentially identical to, the Inglis 1990 and 1991 British applications.

[4] The Falkner priority applications were U.S. Application Serial No. 08/616,313 ("the Falkner '313 application") filed March 14, 1996; and U.S. application Serial No. 08/235,392 ("the Faulkner '392 application"), filed April 29, 1994.

In each, as the moving party, Falkner carried the burden of proof by a preponderance of the evidence. See 37 C.F.R. § 1.637(a); see also Kubota v. Shibuya, 999 F.2d 517, 520 n.2 (Fed. Cir. 1993) (explaining that "[t]he term 'burden of proof' . . . means the burden to establish the proposition at issue by a preponderance of the evidence").

Falkner brought his first preliminary motion pursuant to 37 C.F.R. § 1.633(a),[5] arguing that the claims in Inglis's involved ('040) application that corresponded to the count were unpatentable because they failed to meet the written description requirement of 35 U.S.C. § 112. In support of his argument, he stated, inter alia, that (1) the specification of Inglis's '040 application did not identify any essential genes in poxvirus or describe the inactivation of such genes, (2) vaccines based on vaccinia (a type of poxvirus) had not yet been produced, and (3) the bulk of the Inglis specification was directed not to poxviruses but to herpesviruses. The Board denied Falkner's motion, based in part on his failure to address the perceived shortcomings of the '040 claims in light of the specification.

Second, Falkner moved pursuant to 37 C.F.R. §§ 1.633(g) & 1.637(g) to deny Inglis the priority benefit of his earlier applications, arguing that they did not sufficiently

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[5] On September 13, 2004, the "600" rules expired in favor of new rules found at 37 C.F.R. § 41.100 et seq. However, the Board correctly decided the matter under the old rules, given the parties' reliance on them in filing all motions, oppositions, and replies in the case, which were completed before the new rules took effect. See Singh v. Brake, 222 F.3d 1362, 1371 (Fed. Cir. 2000) (applying a new procedural rule if and only if it did not affect the parties' reliance interests); see also Brown v. Barbacid, 436 F.3d 1376, 1379 n.1 (Fed. Cir. 2006) (holding that the Board did not err in applying the old rules "under which this case was decided").

describe and enable the claims in question.[6] Falkner argued that without the benefit of these applications Inglis would be unable to establish constructive reduction to practice earlier than Falkner. Falkner would win priority as to the count, and Inglis' corresponding claims would be unpatentable. In support of his motion, Falkner alleged deficiencies in Inglis' benefit specifications similar to those raised in his first motion. The Board carefully articulated the legal standard, correctly explaining that "benefit with respect to priority in an interference is granted with respect to counts not claims" and that "[a]ll that is necessary for a party to be entitled to benefit of an earlier filed application for priority purposes is compliance with 35 U.S.C. § 112 with respect to at least one embodiment within the scope of the count." Board Op. at 7 (citing Hunt v. Treppschuh, 523 F.2d 1386, 1389 (CCPA 1975) (holding that where a "parent application is relied upon as a prior constructive reduction to practice[,] . . . . the § 112, first paragraph requirements need only be met for an embodiment within the count")). After careful review of the record, the Board held that Falkner had failed to meet his burden of proof.

Third, Falkner moved for judgment pursuant to 37 C.F.R. § 1.633(a) that the claims in Inglis' involved ('040) application that corresponded to the count were anticipated and therefore unpatentable. He argued that because Inglis' earlier applications had failed to adequately describe and enable the full scope of his current claims, the current claims could not be accorded the benefit of 35 U.S.C. § 120 for the

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[6] Falkner did not argue lack of enablement with respect to the Inglis '963 patent because he believed that the teachings of the Falkner '392 patent, filed in 1994, would have enabled the subsequent '963 patent.

purpose of antedating patent-defeating prior art.[7] The Board explained that 35 U.S.C. §§ 119 & 120 require benefit applications to comply with § 112, first paragraph, with respect to the full scope of what a party now claims, rather than with respect to merely one embodiment within the scope of the interference count. After carefully considering the written description and enablement issues, the Board denied the motion. As a result of the denial of Falkner's several motions, Inglis remained the senior party, and the Board ordered judgment as to the subject matter of the count in favor of Inglis.

D. Issue and Standard of Review

On appeal, Falkner essentially reiterates the arguments that he made before the Board. While we recognize that each of these three arguments is distinct, they are nonetheless all related, and under the facts of this particular case, we need only to resolve the following common issue: whether the Inglis benefit applications adequately describe and enable a poxvirus-based vaccine. Falkner also argues that the Board committed other errors, such as initially designating Inglis as the senior party and failing to afford Falkner an opportunity for briefing prior to making this designation. These arguments lack merit, and we shall not further discuss them. We turn, therefore, to the central issues in this case: written description and enablement.

Written description is a question of fact, judged from the perspective of one of ordinary skill in the art as of the relevant filing date. See Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991). Enablement is a question of law involving underlying factual inquiries. See Genentech, Inc. v. Novo Nordisk A/S, 108 F.3d 1361,

[7] Here, Falkner points to his own U.S. Pat. No. 5,766,882 ("the '882 patent'), issued in March 1995, as the patent-defeating prior art.

1365 (Fed. Cir. 1997); see also In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988) (holding that whether undue experimentation is required is a "conclusion reached by weighing many factual considerations. . . . includ[ing] (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.").

This court applies the standards of the Administrative Procedure Act ("APA") in reviewing decisions of the Board. See Dickinson v. Zurko, 527 U.S. 150, 152 (1999) (holding that 5 U.S.C. § 706 governs our review of PTO appeals). Accordingly, we will set aside actions of the Board if they are arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law, and we set aside factual findings that are unsupported by substantial evidence. See In re McDaniel, 293 F.3d 1379, 1382 (Fed. Cir. 2002) (citing 5 U.S.C. § 706); see also In re Sullivan, 362 F.3d 1324, 1326 (Fed. Cir. 2004) (substantial evidence review of factual findings). We review questions of law de novo. See Rapoport v. Dement, 254 F.3d 1053, 1058 (Fed. Cir. 2001).

Substantial evidence is defined as that which a reasonable person might accept as adequate to support a conclusion. See In re Zurko, 258 F.3d 1379, 1384 (Fed. Cir. 2001). It requires an examination of the record as a whole, taking into account both the evidence that justifies and detracts from an agency's opinion. See In re Gartside, 203 F.3d 1305, 1312 (Fed. Cir. 2000). An agency decision can be supported by substantial evidence, even where the record will support several reasonable but contradictory conclusions. See id.; see also In re Jolley, 308 F.3d 1317, 1320 (Fed. Cir. 2002).

II. DISCUSSION

A. Contents of the Inglis Priority Applications

The claims that correspond to the count of the interference are directed to a novel type of vaccine that is comprised of a "vector virus" in the poxvirus family. Conceptually, poxviruses are a "subgenus" of viruses that includes the "species" vaccinia. All of the prior Falkner applications described poxvirus vaccine vectors in detail, and to the exclusion of other types of vaccine vectors (e.g., herpesvirus vaccine vectors). These applications provided five detailed working examples regarding the preparation and use of vaccines from defective poxviruses. They also described the use of a particular species of poxvirus vaccine vector, namely vaccinia virus.

In contrast, the Inglis applications described vaccine vectors in general, and then focused on the subgenus of herpesviruses, for which they provided a detailed example. Nevertheless, at least three passages discussed the poxvirus invention and specifically mentioned "vaccinia virus."[8] For example, after introducing the concept of vaccine vectors, the specification states that "[t]ypically members of the pox virus family, e.g. vaccinia virus, are used as vaccine vectors."[9] The specification later discusses the deletion of essential genes from vaccine vector genomes, noting that the "invention can

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[8] We recognize that the Inglis applications do not describe any actual reduction to practice of a poxvirus vaccine. See Carroll Declaration (stating that the '040 application did not contain any discussion of the "actual creation of the recited 'mutant poxvirus'" and that the application in fact stated "that a vaccinia virus with a deletion in an essential gene had not been produced."). As we discuss below, however, an actual reduction to practice is unnecessary to satisfy the written description requirement.

[9] Because of the substantial similarity in the specifications of all of the Inglis benefit applications, we shall refer in this opinion to representative passages from the earliest of the applications, the Inglis 1990 British application.

be applied to any virus where one or more essential gene(s) can be identified and deleted from or inactivated within the virus genome" (emphasis added). Moreover, it provides that "the virus may comprise an orthopox virus, for example, vaccinia virus, which may comprise a heterologous sequence encoding an immunogen derived from a pathogen." Finally, it reads:

> For example vaccinia virus, a poxvirus, can carry and express genes from various pathogens, and it has been demonstrated that these form effective vaccines when used in animal experimental systems. The potential for use in humans is vast, but because of the known side effects associated with the widespread use of vaccinia as a vaccine against smallpox, there is reluctance to use an unmodified vaccine in humans. There have been attempts to attenuate vaccinia virus by deleting non-essential genes such as the vaccinia growth factor gene. . . However, such attenuated viruses can still replicate in vivo, albeit at a reduced level. No vaccinia virus with a deletion in an essential gene has yet been produced, but such a virus, deleted in an essential gene as described above, with its complementing cell for growth, would provide a safer version of this vaccine.

The application provides a detailed example of an embodiment that comprised not a poxvirus, but a herpesvirus, including the identity of the deleted essential sequences therein. Nevertheless, for the reasons discussed below, we find no error in the Board's determinations on the adequacy of written description and enablement in the various Inglis disclosures.

B. Enablement

Because the adequacy of the disclosure is judged from the perspective of one of ordinary skill in the art, we start our review of the Board's decision by noting that the parties stipulated to a high level of skill in the art. They defined the skilled artisan as having 5-10 years experience creating recombinant poxvirus, as being familiar with the poxvirus literature, the use of poxvirus as a vector for the expression of heterologous genes, and having the "needed technical skill to practice the experimentation described

in the scientific literature relating to recombinant virus, including poxvirus." The Board agreed with the parties' stipulation as to level of skill.

The Board did not err in finding Inglis' claims to be enabled as a matter of law, in light of its articulated underlying factual findings. In support of its conclusion, it noted that "there is extensive disclosure of the selection of an essential gene, its deletion or inactivation and the production of a mutated virus with said deleted or inactivated gene, albeit for herpesvirus." Moreover, because the differences between the herpesviruses and poxviruses were well known, this would have aided the person of ordinary skill in the art in her application of the lessons of the herpesvirus example in the construction of poxvirus vaccines. The Board observed that "the mere fact that the experimentation may have been difficult and time consuming does not mandate a conclusion that such experimentation would have been considered to be 'undue' in this art. Indeed, great expenditures of time and effort were ordinary in the field of vaccine preparation." Thus, the Board found the Inglis applications to be enabling.

Reviewing the Board's legal conclusion of enablement, as based on its underlying findings of fact, we cannot say that the Board erred. With respect to a skilled artisan's ability to identify "essential" poxvirus genes, as discussed below we note that there was undisputed testimony that as of the time of filing of the earliest Inglis application publications in professional journals had disclosed the DNA sequence of the poxvirus genome along with the locations of the "essential regions." The person of ordinary skill in the art would clearly have possessed such knowledge, and given the ready accessibility of the journals, the absence of incorporation by reference is not problematic. Indeed, "[a] patent need not teach, and preferably omits, what is well

known in the art." Spectra-Physics, Inc. v. Coherent, Inc., 827 F.2d 1524, 1534 (Fed. Cir. 1987).

C. Written Description

On appeal to this court, Falkner essentially reargues the positions on written description that he took before the Board. Although the Board erred in its articulation of the written description standard, that error is harmless. The Board held that "an actual possession standard is not required." (emphasis added). But our precedent clearly establishes that "[t]he applicant must . . . convey to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention." Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991). Nonetheless, we conclude there is no need for remand because the undisputed testimony supports the Board's ultimate conclusion.

As noted above, the Board found several passages in the Inglis '040 application (and in the benefit applications) that were directed to poxvirus. No length requirement exists for a disclosure to adequately describe an invention. See In re Hayes Microcomputer Prods., Inc. Patent Litig., 982 F.2d 1527, 1534 (Fed. Cir. 1992) ("[T]he adequacy of the description of an invention depends on its content in relation to the particular invention, not its length."). Furthermore, the testimony of Falkner's expert, Dr. Boursnell, established that the articles describing essential genes for poxvirus were well-known in the art. Dr. Boursnell testified that "the skilled person would have been readily able to choose an essential vaccinia gene" based on references that have been publicly available since 1990. The testimony of Inglis' expert, Dr. Carroll, did not refute this claim.

The parties also dispute several aspects of our law of written description, which we now address. We conclude that the Board applied correct law. Specifically, we hold, in accordance with our prior case law, that (1) examples are not necessary to support the adequacy of a written description (2) the written description standard may be met (as it is here) even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure.

1. Examples Are Not Required

First, it is clear that the absence of examples involving poxviruses in the Inglis applications does not render the written description inadequate. As we explained in LizardTech, Inc. v. Earth Resource Mapping, PTY, Inc.:

> A claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. That is because the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before. Placed in that context, it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation.

424 F.3d 1336, 1345 (Fed. Cir. 2005) (citing Union Oil Co. v. Atl. Richfield Co., 208 F.3d 989, 997 (Fed. Cir. 2000); In re GPAC Inc., 57 F.3d 1573, 1579 (Fed. Cir. 1995)).

2. Actual Reduction to Practice Is Not Required

As we explained in Capon v. Eshhar, "[t]he 'written description' requirement implements the principle that a patent must describe the technology that is sought to be patented; the requirement serves both to satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the

patentee was in possession of the invention that is claimed." 418 F.3d 1349, 1357 (Fed. Cir. 2005). The Board was correct, however, not to view as dispositive that Inglis had not actually produced a poxvirus vaccine,[10] because an actual reduction to practice is not required for written description.[11] See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 926 (Fed. Cir. 2004) ("We of course do not mean to suggest that the written description requirement can be satisfied only by providing a description of an actual reduction to practice. Constructive reduction to practice is an established method of disclosure . . . ."). Rochester, moreover, is consistent with Supreme Court precedent. In the context of interpreting 35 U.S.C. § 102(b), the Court held that "[t]he word 'invention' must refer to a concept that is complete, rather than merely one that is 'substantially complete.'" Pfaff v. Wells Elecs., 525 U.S. 55, 66 (1998). It then proceeded to make clear that although "reduction to practice ordinarily provides the best evidence that an invention is complete. . . . it does not follow that proof of reduction

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[10] The Inglis specifications stated that "[n]o vaccinia virus with a deletion in an essential gene has yet been produced, but such a virus, deleted in an essential gene as described above, with its complementing cell for growth, would provide a safer version of this vaccine."

[11] The Board believed that Falkner's expert, Dr. Carroll, had premised his opinions on the misunderstanding that actual reduction to practice was required to prove written description, and it discredited his expert opinion.

to practice is necessary in every case." Id. (emphasis added).[12] Thus, to the extent that written description requires a showing of "possession of the invention," Capon, 418 F.3d at 1357 (emphasis added), Pfaff makes clear that an invention can be "complete" even where an actual reduction to practice is absent.[13] The logical predicate of "possession" is, of course, "completeness."

3. Recitation of Known Structure Is Not Required

Falkner argues, inter alia, that the Inglis specifications do not adequately describe the poxvirus invention, in light of Eli Lilly, because they do not describe the "essential regions" of any poxvirus. 119 F.3d 1559. We note, in addition, that Inglis did not attempt to incorporate by reference any literature that described the DNA sequence of the poxvirus genome and the locations of the "essential regions." However, it is the binding precedent of this court that Eli Lilly does not set forth a per se rule that whenever a claim limitation is directed to a macromolecular sequence, the specification must always recite the gene or sequence, regardless of whether it is known in the prior art. See Capon, 418 F.3d at 1357 ("None of the cases to which the Board attributes the requirement of total DNA re-analysis, i.e., Regents v. Lilly, Fiers v. Revel, Amgen, or

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[12] Similarly, this court has carefully explained the relationship between written description and possession, explaining that a showing of possession is not necessarily sufficient to demonstrate the adequacy of written description. See, e.g., Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 1330 (Fed. Cir. 2002) ("[P]roof of a reduction to practice, absent an adequate description in the specification of what is reduced to practice, does not serve to describe or identify the invention for purposes of § 112, P 1. As with 'possession,' proof of a reduction to practice may show priority of invention or allow one to antedate a reference, but it does not by itself provide a written description in the patent specification.").

[13] In contrast to reduction to practice, conception is a prerequisite to an adequate written description. See Fiers v. Sugano, 984 F.2d 1164, 1171 (Fed. Cir. 1993) ("[O]ne cannot describe what one has not conceived.").

Enzo Biochem, require a re-description of what was already known."). Thus, "[w]hen the prior art includes the nucleotide information, precedent does not set a per se rule that the information must be determined afresh." Id. at 1358. Rather, we explained that:

> The descriptive text needed to meet these requirements varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence. The law must be applied to each invention that enters the patent process, for each patented advance is novel in relation to the state of the science. Since the law is applied to each invention in view of the state of relevant knowledge, its application will vary with differences in the state of knowledge in the field and differences in the predictability of the science.

Id. at 1357.

Indeed, a requirement that patentees recite known DNA structures, if one existed, would serve no goal of the written description requirement. It would neither enforce the quid pro quo between the patentee and the public by forcing the disclosure of new information, nor would it be necessary to demonstrate to a person of ordinary skill in the art that the patentee was in possession of the claimed invention. As we stated in Capon, "[t]he 'written description' requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution." Id. at 1358. Indeed, the forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification. Accordingly we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here "essential genes"), satisfaction of the written description requirement does not

require either the recitation or incorporation by reference[14] (where permitted) of such genes and sequences.

In conclusion, having reviewed the decision of the Board, we can discern no error in its conclusion that the disclosures relied upon by Inglis for priority purposes adequately described and enabled the invention directed to poxvirus, there being substantial evidence to support these findings. Consequently, we hold that the Board's award of priority to Inglis was proper.

AFFIRMED

No costs.

[14] Here, the patentee did not attempt incorporation by reference. Where, of course, certain material that is not present in the specification is deemed nonessential to the satisfaction of the written description requirement, the issue of proper incorporation by reference vel non is irrelevant.